จุฬาลงกรณ์มหาวิทยาลัย

เงินอุดหนุนงบประมาณแผ่นดิน

รายงานผลการวิจัย

ชื่อเรื่อง

Hematological abnormalities in oral lichen planus, recurrent aphthous ulceration and stomatitis or glossitis

โดย

กอบกาญจน์ ทองประสม
พรพรรณ ยวงนาค
วิไลวรรณ อเนกสุข

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กิตติกรรมประกาศ (Acknowledgement)

งานวิจัยนี้ได้รับเงินสนับสนุนจากเงินอุดหนุนงบประมาณแผ่นดินปี 2541

คณะผู้วิจัยขอขอบพระคุณ ศาสตราจารย์ นายแพทย์ ดร.สุวิทย์ อารีกุล ภาควิชารังสีไอโซโทป คณะเวชศาสตร์เขตร้อน มหาวิทยาลัยมหิดลที่ให้การปรึกษาแนะนำในการวิจัยครั้งนี้

ขอขอบคุณ คุณเจริญ บุญจตุรัส ที่ได้ช่วยเจาะเลือดผู้ป่วยและเก็บข้อมูลตลอดการวิจัย

ขอบคุณข้าราชการภาควิชาเวชศาสตร์ช่องปากทุกท่านตลอดจนผู้ป่วยที่ให้ความร่วมมือในการศึกษาวิจัยและ Miss Petra Hirch ที่ช่วยแก้ไขบทความนี้ให้สมบูรณ์

ชื่อโครงการวิจัย ความผิดปกติของโลหิตในผู้ป่วยไลเคนพลานัสในช่องปาก แผลร้อนในและอาการอักเสบในช่องปากหรือลิ้นอักเสบ

ชื่อผู้วิจัย กอบกาญจน์ ทองประสม , พรพรรณ ยวงนาค และ วิไลวรรณ อเนกสุข

เดือนและปีที่ทำวิจัยเสร็จ กันยายน 2541

บทคัดย่อ

จุดมุ่งหมายของการศึกษานี้ เพื่อวิเคราะห์สภาวะของโลหิตในผู้ป่วยที่มีรอยโรคไลเคนพลานัสในช่องปาก แผลร้อนในและอาการอักเสบในช่องปากหรือลิ้นอักเสบ จากการตรวจหาความผิดปกติของโลหิตในผู้ป่วยทั้งหมดจำนวน 61 ราย โดยตรวจหาระดับซีรั่มโฟเลตโฟเลตในเม็ดโลหิตแดง และระดับซีรั่มไวตามินบี 12 โดยแบ่งกลุ่มผู้ป่วยออกเป็น 3 กลุ่ม คือผู้ป่วยไลเคนพลานัสในช่องปาก 22 ราย ผู้ป่วยแผลร้อนใน 19 ราย และผู้ป่วยที่มีการอักเสบในช่องปากหรือลิ้นอักเสบ 20 ราย จากผลการศึกษาพบว่าระดับโฟเลทในเม็ดโลหิตแดงและซีรั่มโฟเลตที่ต่ำกว่าปกติพบในผู้ป่วยไลเคนพลานัสในช่องปากจำนวน (11/22), แผลร้อนใน (11/19) และผู้ป่วยที่มีอาการอักเสบในช่องปากหรือลิ้นอักเสบ (8/20) ราย อย่างไรก็ตามไม่พบการแตกต่างของการพร่องของระดับโฟเลตระหว่างกลุ่มต่างๆ อย่างมีนัยสำคัญทางสถิติ ($P > 0.05$) ระดับซีรั่มไวตามินบี12 ที่ต่ำกว่าปกติ พบเพียง 5 ใน 61 รายเท่านั้น ความผิดปกติของระบบทางเดินอาหารพบ 15 รายในผู้ป่วยกลุ่มนี้ การรักษาผู้ป่วยที่มีความบกพร่องต่างๆพบว่ามีการตอบสนองที่ดีประมาณ 46.3% ของผู้ป่วยทั้งหมด โดยสรุปการตรวจหาระดับโฟเลตและไวตามินบี$_{12}$ เป็นสิ่งที่แนะนำให้ควรทำในผู้ป่วยที่มีรอยโรคในช่องปากที่รักษายากเพื่อผลดีต่อการรักษา

คำสำคัญ โฟเลต , ความผิดปกติของระบบทางเดินอาหาร , ลิ้นอักเสบ , ไลเคนพลานัสในช่องปาก , แผลร้อนใน , การอักเสบในช่องปาก , ไวตามินบี$_{12}$

Project Title Hematological abnormalities in oral lichen planus , recurrent aphthous ulceration and stomatitis or glossitis

Name of the Investigators Thongprasom K., Youngnak P. and Aneksuk V.

Year 1998

Abstract

Objective. The aim of this study was to analyse the hematologic status in Thai patients with oral lichen planus (OLP), recurrent aphthous ulceration (RAU) and stomatitis or glossitis (ST/GT).

Study design. Sixty one patients were examined consecutively for hematological abnormalities including serum folate, red cell folate and serum vitamin B_{12} levels. The patients were divided into 3 major groups with OLP(22), RAU(19) and ST/GT(20).

Results. Low red cell folate and low serum with red cell folate were found in patients with OLP (11/22), RAU (11/99) and ST/GT (8/20). However, there was no statistically significant difference in folate deficiencies among these groups ($P>0.05$). Low serum vitamin B_{12} levels were found in only 5 of 61 cases. Gastrointestinal disorders were found in 15 of all these groups. Treatment in patients with deficiencies showed good response in approximately 46.3% of the cases.

Conclusions. Investigations for folate and vitamin B_{12} levels are recommended in patients with refractory oral lesions for the benefit of treatment.

Key words: folate, gastrointestinal disorders, glossitis, oral lichen planus, recurrent aphthous ulceration, stomatitis, vitamin B_{12}.

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Introduction

It has been recognised that hematological disorders can affect the oral mucosa as in recurrent aphthous ulceration (RAU), glossitis (GT), stomatitis (ST) and angular cheilitis.[1,2] The oral changes may occur in the absence of abnormalities in complete blood count (CBC), and all may be without gastrointestinal complaints.[3] It may be difficult to establish whether the oral lesions are directly due to the underlying disease or reflect a hematologic deficiency. However, it has been suggested that iron, vitamin B_{12} or folic acid deficiency might play a direct role in the pathogenesis of RAU.[4] Furthermore, in one study the prevalence of hematological abnormalities in the erosive oral lichen planus (OLP) group was significantly greater than in the non-erosive group.[5] However, opinions diverge as to whether a full blood screening procedure, including serum folate, red cell folate and vitamin B_{12} determination, is mandatory in each case. The significance of hematological abnormalities in oral manifestations is still unclear and controversy remains about the need for full hematologic assessment in patients with ST, GT, RAU, OLP etc.

The purpose of our study was to determine the full hematologic status and levels of red cell folate, serum folate and vitamin B_{12} in a series of consecutive patients with refractory OLP, RAU and ST/GT. The relationship between the underlying causes of these oral manifestations was also investigated for the benefit of treatment.

Patients and methods

Sixty one patients referred to the Oral Medicine Department, Faculty of Dentistry, Chulalongkorn University between 1996 and 1999 with oral symptoms and lesions were admitted to this study. The patients were divided into 3 groups.

A. Oral lichen planus (OLP). This group consisted of 22 patients with erosive and atrophic oral lichen planus diagnosed by the clinical manifestations and histopathological examination.

B. Recurrent aphthous ulceration (RAU). Nineteen patients with histories of oral ulceration recurring within 3 months were studied. All cases had more than one site of the lesion and had been diagnosed as minor type but not herpetiform type.

C. Stomatitis or glossitis (ST/GT). This group consisted of 20 patients who primary complained of a sore mouth, discomfort in the tongue without lesions, or whose lingual mucosa was erythematous or atrophic and in whom candida infection had been excluded. This group included 2 patients with severe atrophic glossitis, 4 patients with foliate papillitis and 14 patients with no specific oral signs except for a burning sensation.

In all patients, the types of the lesions, the duration of symptoms, medication, gastrointestinal disorders, and systemic diseases were recorded.

Verbal consent was obtained from all patients before drawing venous blood. Samples were taken between 10 a.m and 12 a.m in an attempt to minimise the effects of diurnal variation.

Hematological investigations were carried out in all patients, consisting of a full blood count and determination of hemoglobin (Hb), folate and vitamin B_{12} status. Serum folate, red cell folate and serum B_{12} each was determined by competition binding radioassay . Hemoglobin typing was analysed by electrophoresis.

Normal laboratory ranges in Thai patients were: serum folate 5-24 ng/ml, red cell folate 221-1113 ng/ml, serum B_{12} 211-911 pg/ml, MCV (M = 82.2-99.5, F = 80-94 fl),Hb (M =13-18, F = 11-16)g/dl, Hct (M = 35-49, F = 32-42)%.*

Results

The characteristics of the 61 patients, duration of diseases at presentation and associated conditions are shown in Table 1. The age range of the patients in this study was 16-79 years (mean = 44.18 $\pm$ SD 16.44). The duration of diseases varied from 0.1-175 months (mean = 37.22 $\pm$ SD 38.91). Systemic conditions were found in 28 out of 61 cases whereas 21 patients were taking medications. Thirty out of 61 patients showed evidence of red cell folate and serum with red cell folate deficiencies (Table 2). Low red cell folate and low serum with red cell folate were found in patients with OLP (11/22). Three out of 61 patients had low hemoglobin (1/22 case in the OLP group and 2/20 cases in the ST/GT group). Furthermore, patients with low MCV were found in the OLP group (5/22) and in the ST/GT group (2/20). OLP patients with folate deficiencies were treated with folic acid, (5 mg twice daily) together with 0.1% FAO for 3 months, after which the lesions showed improvement (Fig. 1a,b). In the RAU group, patients with folate deficiencies (11/19) were also treated with 0.1% FAO , folic acid and the underlying diseases such as peptic ulceration or gastritis were corrected(Fig.2a,b). Patients with RAU who had no underlying diseases also showed a good response after treatment with folic acid and 0.1% FAO. In the ST/GT group, folate deficiencies were found in 8/20 cases. They also showed good response after treatment with folic acid 5 mg two or three times daily for more than 6 months. Low folate levels in

* Value from Radioisotope Department, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

all cases showed an approximately 46.34% response rate to the treatment with folic acid (5 mg) (Table 3).

Low serum vitamin B_{12} levels were found in only 5/61 cases in this study. Low serum vitamin B_{12} was found in 2 cases in the ST/GT group and the patients showed a dramatic response after treatment with hydroxocobalamin injections for 2 weeks (Fig. 3a,b, 4a,b).

However, according to the Chi Square Test there was no statistically significant difference between the folate deficiences in these groups ($P>0.05$). All cases showed normal red blood cell indices except for one case in the OLP and two cases in the ST/GT group with low hemoglobin, hematocrit and mean cell volume. Moreover, the investigations for serum iron and TIBC were normal. Some patients had laboratory reports of anemia but oral examination did not show any oral mucosal changes. All patients in the RAU group showed a normal peripheral blood picture except for two cases with high MCV. Gastrointestinal disorders were found in 15 of the 61 cases (24.59 %) in this study (Table 4).

Discussion

In our study, the deficiencies in red cell folate and serum with red cell folate were associated with unknown etiology (14), medications (5), gastrointestinal disorders such as gastritis and peptic ulceration (7), Hb E traits (3) and β - thalassemia (1) which differs from the results of a previous study.[2] In the OLP group, patients with hemoglobin abnormalities such as Hb E traits 3 cases showed serum folate and serum with red cell folate deficiencies. In all of these cases, hemoglobin and hematocrit were normal but the MCV was decreased. A previous study reported that Thai patients with β - thalassemia had low serum folate (3.3%) and low red cell folate (84%) as compared with the normal range in Thai people.[6] These

findings could explain that due to impaired globin synthesis the red blood cells are increasingly destroyed. However, one case with homozygous Hb E disease showed low hemoglobin, hematocrit, MCV and serum vitamin B_{12} but red cell folate and serum folate were normal.

In severe cases of OLP combined treatment with folic acid (5 mg) and a potent topical steroid (0.1% fluocinolone acetonide in orabase) was found useful in some cases but the lesions recurred after discontinuation of these medications. The refractory OLP patients may indicate a lack of DNA, RNA and protein synthesis and hence diminished epithelium proliferation resulting in the oral mucosal epithelium not to heal or to show no response to the treatment.

In our study patients with RAU showed deficiencies in red cell folate and serum with red cell folate in 11 out of 19 cases. This group consisted of 6 cases with unknown etiology, 2 cases with gastrointestinal disorders, 1 case with β - thalassemia trait, 1 case with Hb E trait and 1 case with medication. Interestingly, patients who had no medical history or had not taken any medications still had RAU for a long period and folate deficiencies. Our findings differ from the results of an other study which showed a minority of patients with deficiencies of folate levels.[7] This might be because our RAU cases were referred and hence,we received many of the worst cases.

However, the report of a low serum vitamin B_{12} value along with impaired B_{12} absorption improved by the addition of an intrinsic factor in the absence of blood changes indicates severe atrophic gastritis.[8] One case with low serum vitamin B_{12} had undergone tumor gastrectomy 5 years previously before complaining of stomatitis and glossitis over the course of 3 months. Actually, vitamin B_{12} is stored in the liver and , if absorption ceases, stores are sufficient to sustain requirements for several years.[9] When the bone marrow stores of vitamin B_{12} are depleted, there is no longer enough vitamin B_{12} for normal DNA synthesis.

When this deficiency progresses to stage IV negative balance, overt clinical anemia appears. Thus, to wait for clinical anemia to occur before looking for vitamin B_{12} deficiency will result in many patients with severe cognitive dysfunction.[10] Atrophic gastritis, damaged gastric mucosa and gastric atrophy, including loss of gastric acid and IF secretion can diminish vitamin B_{12} absorption.[11, 12, 13] In this case of tumor gastrectomy, there was a dramatic response after treatment with (1,000 micrograms) hydroxocobalamin (intramuscular injection) twice weekly for 2 months and once a month thereafter. The burning sensation was relieved within 2-3 days; regeneration of tongue papillae returned to normal by 2 weeks. During a two year follow-up, oral vitamin B_{12} (300 micrograms daily) was administered for maintenance; there were neither clinical side-effects such as toxicity, nor increased cost. Thus the recommendations for initial and maintenance therapy of vitamin B_{12} deficiency states are 5 or 6 biweekly injections for loading, an injection once a month for maintenance, followed by oral therapy similar to those stated in a previous study.[14] Moreover, this patient had no recurrence of signs or symptoms in the oral cavity. In contrast, 3 patients taking vitamin B complex had shown high levels of serum vitamin B_{12} but still had a burning sensation and glossitis. Further studies performed on a larger group are required for better clarification.

However, the frequency of oral lesions such as angular cheilitis, lichen planus, aphthous ulceration, glossitis etc. showed no correlation with inflammatory bowel diseases [15].We suggest routine hematologic screening to be performed in all patients, especially in cases with no response to medications. It is necessary to investigate the folate and vitamin B_{12} levels even in the face of an apparently normal peripheral blood picture. The underlying causes associated with oral manifestations should also be detected for correction. An accurate hematological assessment is considered important in the diagnosis and management. Some patients with gastrointestinal disorders who showed no response to treatment of those

deficiencies should be further studied in large groups and be kept under long-term observation. Hence, patients with or without underlying diseases and prolonged oral manifestations should be investigated for folate and vitamin B_{12} levels for elucidating the underlying causes and correcting these deficiencies for the benefit of treatment and management in all cases.

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Table 1. Sex and age of patients, duration of disease at presentation and associated conditions

Group	N	Sex		Age (yrs.) mean ± SD (range)	Duration of disease (mons.) mean ± SD (range)	Associated conditions*(cases)	
		F	M			Systemic conditions	Medications
Oral lichen planus	22	19	3	48.27 ± 17.50 (16- 79)	41.09 ± 44.12 (1-175)	HbE traits (3) Diabetes mellitus(3) Hypertension(2) GI disorder (2) Homozygous Hb E disease(1) Hepatitis B (1)	Estrogen (3) Hypoglycemic (2) Antihypertensive (2) Vitamin B complex (2) Antithyroid (1) Antacids (1) Hypolipidemia (2)
Recurrent aphthous ulceration	19	14	5	34.16 ± 10.23 (22-53)	46.16 ±38.29 (4 -120)	GI disorders (5) β - thalassemia traits (2) HbE trait (1) Turner's syndrome(1) Atopic(1) Migraine(1)	Estrogen (1) Antihistamines (2) Ergotamine tartrate(1)
Stomatitis or glossitis	20	15	5	49.20 ± 16.41 (21-74)	23.80 ± 30.54 (0.1-120)	GI disorders (7) Hypertension(1)	Vit. B complex (4) Hypolipidemia (2) Antacids (1) Antihypertensive(1)
Total	61	48	13	44.18 ± 16.44 (16-79)	37.22 ± 38.91 (0.1-175)	28	21

* Some patients had more than one systemic condition and were taking more than one medication.

Table 2. Hematological abnormalities in patients with OLP, RAU and ST/GT

Group	No	Low Folate			Low Vitamin B_{12}	Hb↓	MCV	
		Serum	RBC	Serum+RBC			↓	↑
OLP	22	5	6	5	2	1	5	1
RAU	19	5	8	3	1	-	-	2
ST/GT	20	1	6	2	2	2	2	-
Total	61	11	20	10	5	3	7	3

Table 3. Treatment with folic acid in patients with low folate levels.

Group	No.	response	no response	dropped out
OLP	16	8	3	5
RAU	16	5	-	11
ST/GT	9	6	1	2
Total	41	19	4	18

Table 4. Relationship between gastrointestinal disorders and patients with OLP, RAU and ST/GT.

Group	No.	GI disorders						Total GI disorders (%)	No GI disorders (%)
		Peptic ulcer		Gastritis		Operation*			
		case	duration (yrs.)	case	duration (yrs.)	case	duration (yrs.)		
OLP	22	1	5	1	-	-	-	2 (9.09)	20 (95.24)
RAU	19	2	1-18	2	10	2	2	6 (31.58)	13 (72.22)
ST/GT	20	4	2-20	2	5-10	1	5	7 (35)	13 (65)
Total	61	6	2-20	4	5-10	3	2-5	15 (24.59)	46 (77.97)

* Appendectomy, gastrectomy (tumor), small intestine

Figure legends

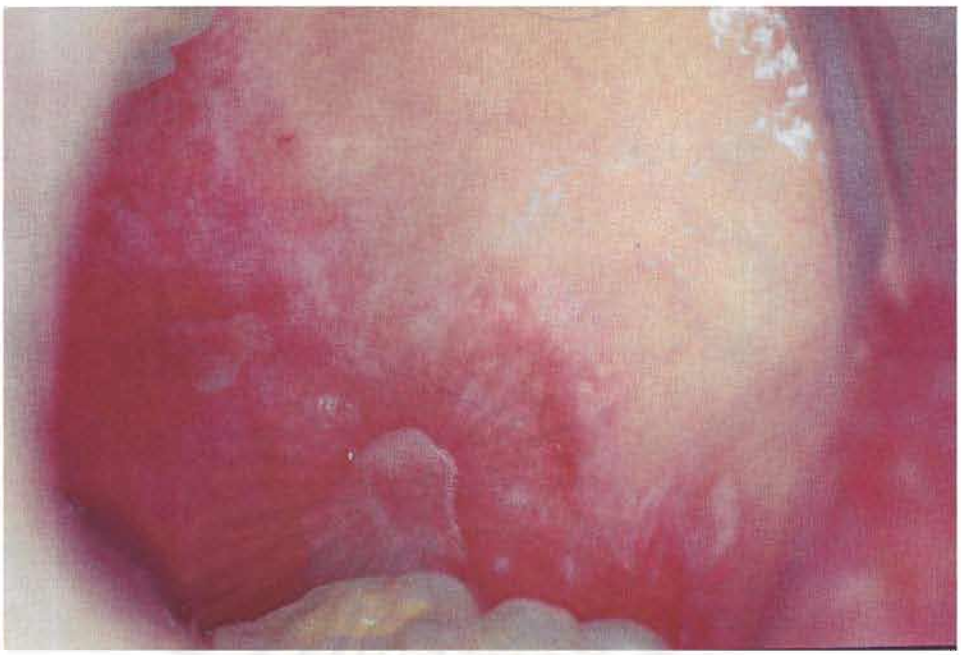


Fig.1a OLP lesion on the left buccal mucosa before treatment.

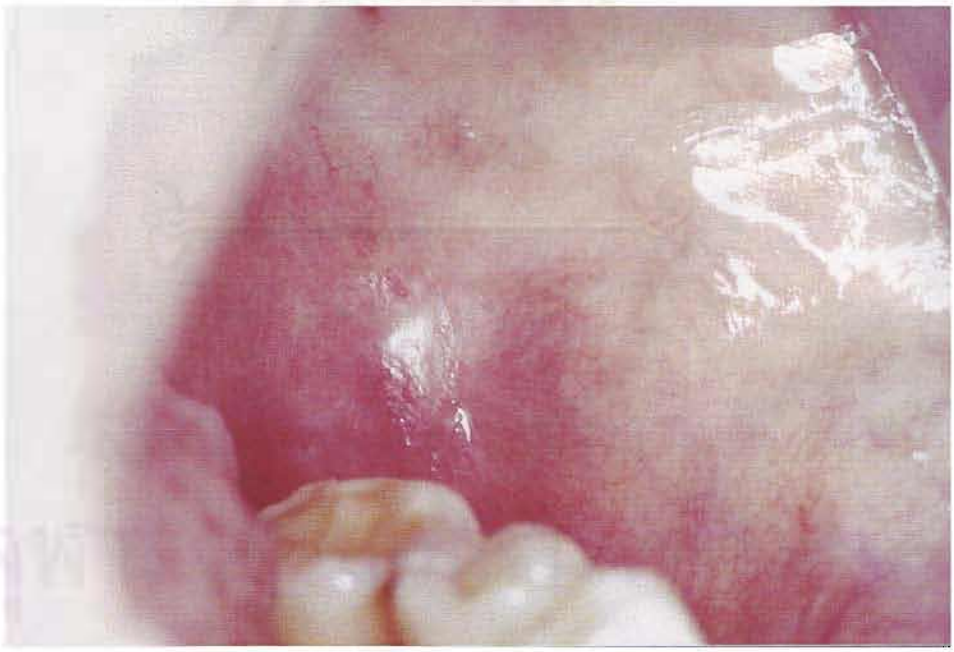


Fig.1b After treatment with folic acid 5 mg. twice a day together with 0.1% FAO for 3 months, the OLP lesion on the buccal mucosa showed significant improvement.

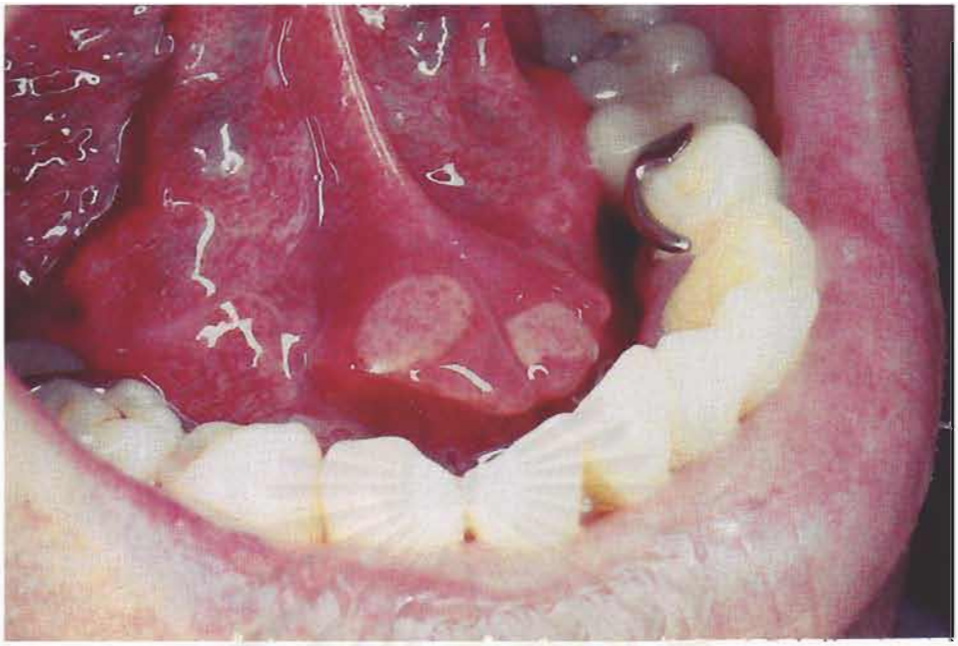


Fig. 2a RAU at the floor of the mouth before treatment.

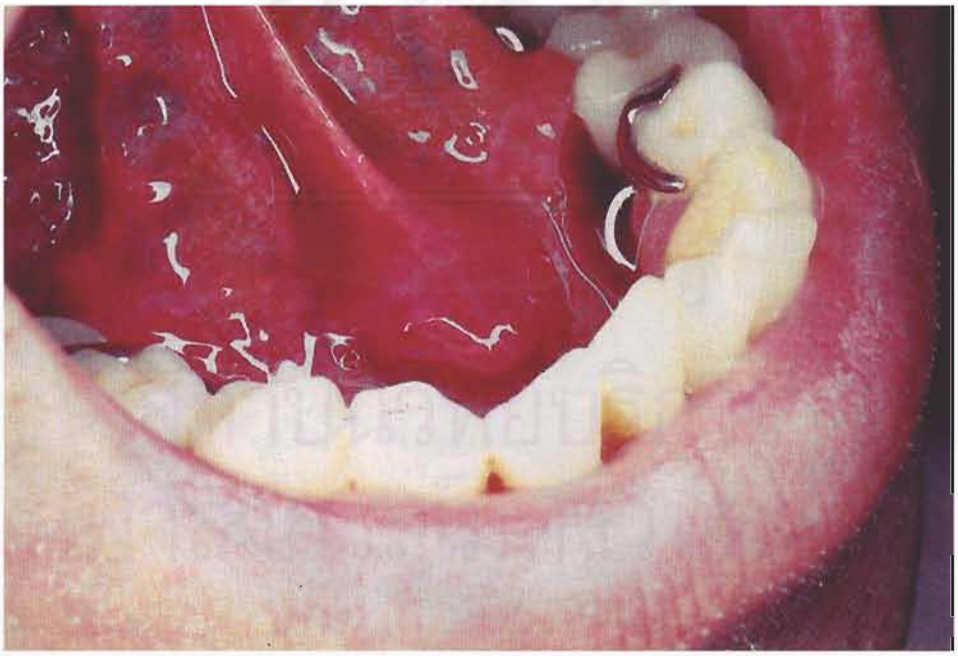


Fig.2b After elucidating the underlying disease and RAU was treated with 0.1% FAO, the ulceration showed complete remission and no recurrence.

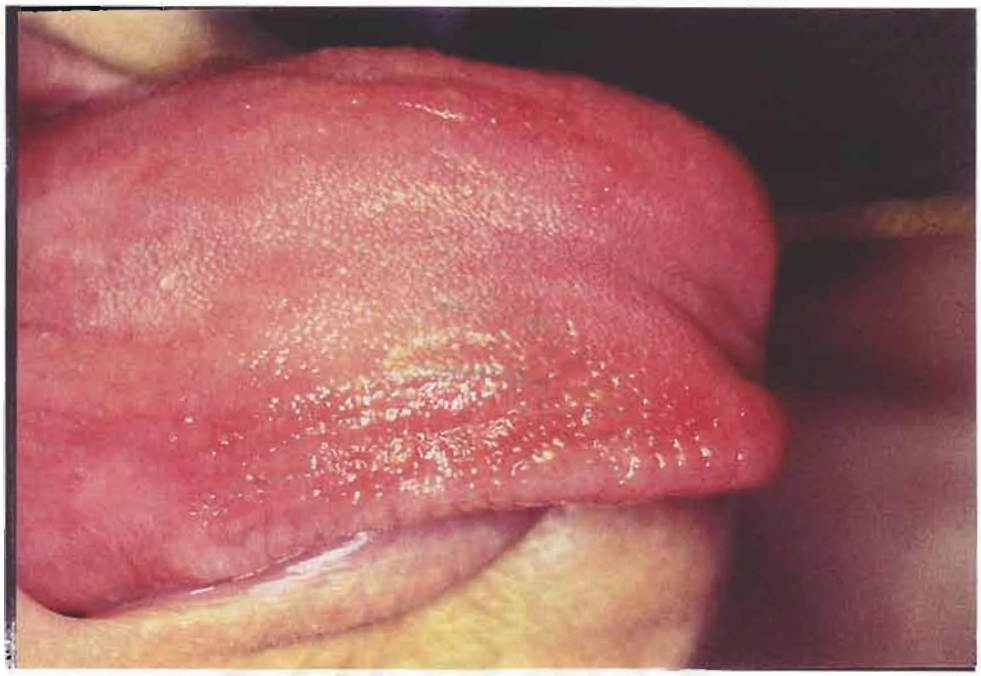
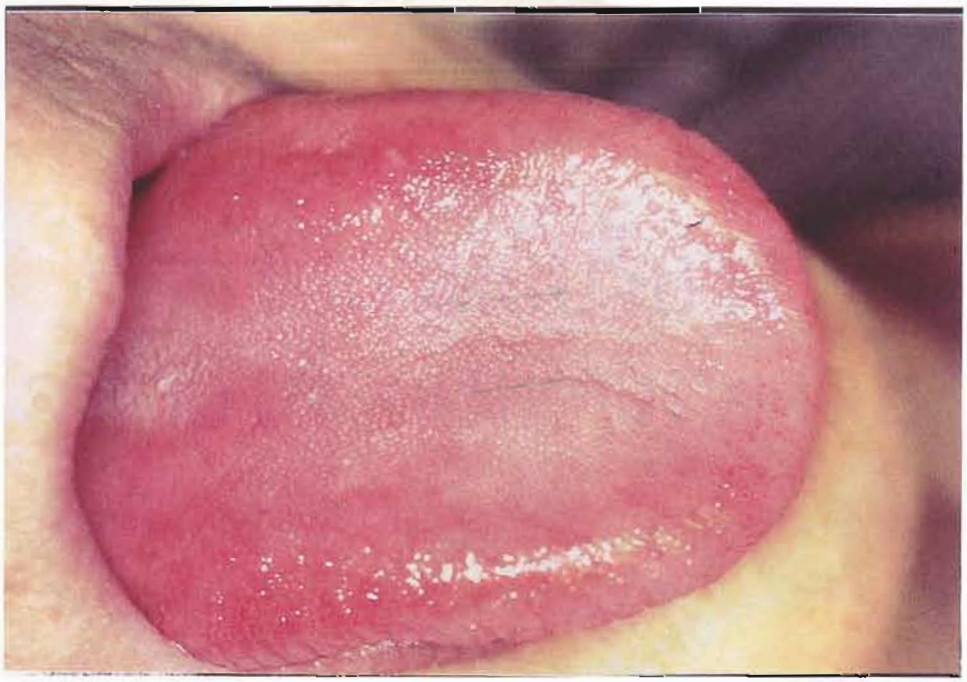


Fig. 3 Fiery red tongue with filiform papillae atrophy before treatment

a) the right lateral



b) the dorsum of the tongue

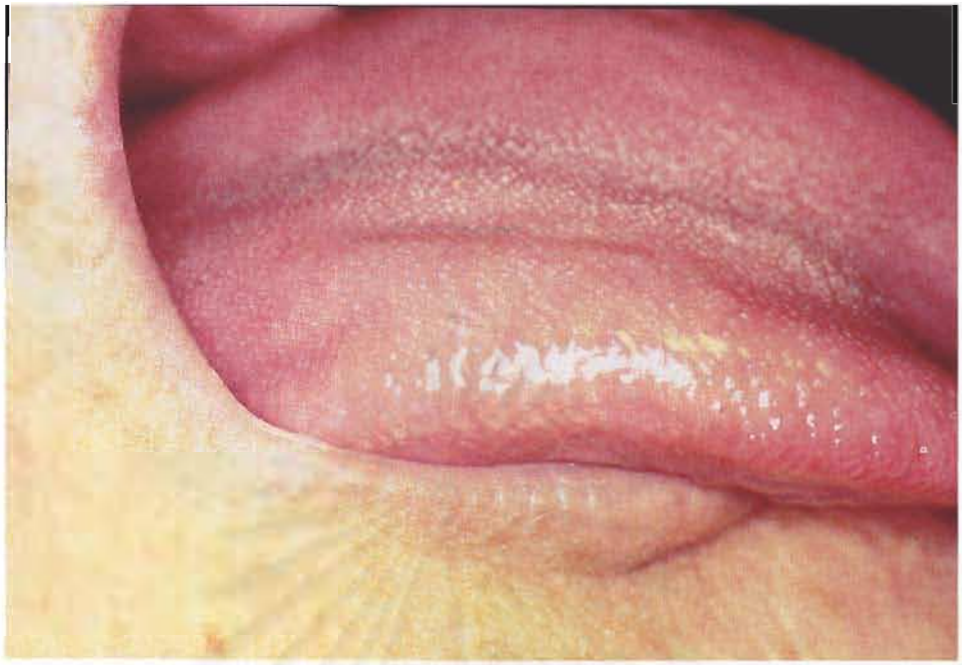
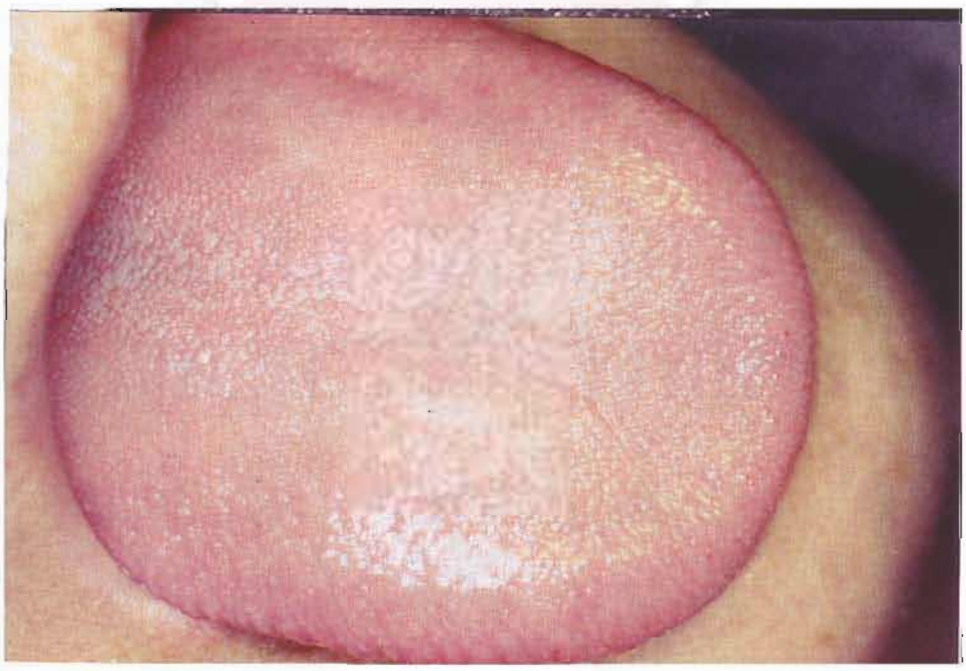


Fig. 4 After treatment with 1,000 micrograms hydroxocobalamin intramuscular injection twice a week for 2 weeks the tongue returned to normal.

a) the right lateral



b) the dorsum of the tongue

Sex, age, serum folate, red cell folate serum vitamin B_{12} level duration of symptoms and associated conditions in OLP patients.

No.	Sex	Age	Serum folate (5-24ng/ml)	Red cell folate (221-1113ng/ml)	Vit B_{12} (211-911pg/ml)	duration (mons.)	associated conditions	
							systemic conditions	medications
1	F	34	11.52	-	375	31	-	-
2	F	52	42.6	-	227	20	-	antacid
3	F	57	**3.6**	**109**	405	117	-	estrogen hormone
4	F	69	11.42	**168**	**202**	36	-	glucophage
5	M	52	**4.2**	289	626	47	-	-
6	F	69	23.69	**75**	**1320**	9	-	-
7	M	31	**3.05**	**86**	359	108	-	-
8	F	24	**3.84**	393	320	2	peptic ulcer	-
9	F	32	8.76	**149**	224	1	-	contraceptive injection
10	F	41	10.86	290.64	278	62	-	antithyroid (eltroxin)
11	F	53	**4.32**	305	416	62	HbE trait DM	hypoglycemic drug
12	F	16	**1.64**	534	230	12	-	* lesion หลังจาก crown #21
13	F	18	**1.30**	**131.96**	775	12	Hb E trait	-
14	F	42	12.49	**218**	292	29	-	-
15	M	60	**32.41**	374	243	75	Triglyceride สูง Hypertension Hepatitis	antihypertensive hypolipidemia drug
16	F	49	17.43	**163**	559	36	-	estrogen hormone
17	F	62	**48.89**	**1,361**	395	175	-	-

18	F	75	**3.23**	245	**1,062**	8	DM Hypertension	antidepressant hyperglycemic antihypertensive
19	F	49	15.08	222	**199**	24	Rheumatoid arthritis Homozygous HbE disease	-
20	F	54	5.92	**158**	468.7	24	Hb E trait	vitamin B complex hypolipidemia drug
21	F	79	4.39	**31**	386.4	12	-	vitamin B complex
22	F	44	**3.7**	30	**701.4**	2	-	*exposed Zinc phosphide

Sex, age serum folate, red cell folate, serum vitamin B_{12} level ,duration of symptoms and associated conditions in RAU patients.

No.	Sex	Age	Serum folate (5-24ng/ml)	Red cell folate (221-1113ng/ml)	Vit B_{12} (211-911pg/ml)	duration (mons.)	associated conditions	
							systemic conditions	medications
1	M	42	**3.7**	-	682	36	small intestine dissection	-
2	M	43	**2.52**	-	558	24	-	-
3	M	52	6	-	562	5	appendicectomy	-
4	F	40	6.8	**214**	289	12	Hb E trait, Turner's syndrome	Microganon Atenolol
5	F	27	**3.9**	301	598	48	gastritis	-
6	F	36	7.07	**149**	481	60	gastritis	-
7	F	23	**2.52**	**193**	425	60	-	-
8	F	23	6.24	**199**	319	4	-	-
9	F	23	6.20	**158**	612	120	-	-
10	F	22	**3.88**	**198**	481	60	-	-
11	F	32	20.11	**85**	**974**	4	-	-
12	F	23	**4.42**	275	287	120	β - thalasemia	-
13	F	25	5.25	**164**	477	120	β - thalasemia	-
14	M	53	6.01	563	429	60	peptic ulcer	-
15	F	39	5.47	1,085	303	48	-	-
16	F	29	**4.52**	**154**	714	24	-	-
17	F	36	**27.06**	**207**	879.9	24	Atopic	Vit FBC, Dimetap
18	F	33	**3.30**	299	600.4	36		-
19	M	48	10.48	58.91	208	12	Migraine, peptic ulcer	Cafergot

Sex, age, serum folate, red cell folate, serum vitamin B_{12} level , duration of symptoms and associated conditions in stomatitis/glossitis patients.

No.	Sex	Age	Serum folate (5-24ng/ml)	Red cell folate (221-1113ng/ml)	Vit B_{12} (211-911pg/ml)	duration (mons.)	associated conditions	
							systemic conditions	medications
1	F	66	**25.8**	-	**144**	3	gastrectomy	-
2	M	69	10.08	-	248	84	peptic ulcer	-
3	F	57	9.24	-	452	3	-	-
4	M	72	**25.68**	-	**1,558**	24	-	Vit B complex
5	F	36	14.52	-	882	14	-	-
6	F	28	**4.3**	-	275	12	-	-
7	F	60	**39**	-	**1,263**	-	-	Vit. B complex
8	F	40	14.88	**208**	669	0.1	-	-
9	M	42	5.4	250	439	36	peptic ulcer	-
10	F	39	13.08	-	781	2	-	Vit. B complex
11	F	31	**0.72**	**180**	**403**	17	hemorrhagic gastritis	antacid
12	M	48	10.48	**58.91**	**208**	12	peptic ulcer	-
13	M	74	11.85	237	408	9	-	hypolipidemia drug
14	F	74	11.74	**103**	343	5	gastritis	-
15	F	49	20.4	**189**	**1,806**	3	peptic ulcer	Vit. B complex
16	F	21	**26.65**	**115**	**1,137.3**	36	-	-
17	F	47	10.56	**182**	363.6	120	anemia, cataract	-
18	F	57	17.72	463	589	12	hypertension	Dichloride, hypolipidemia
19	F	28	5.53	**81**	463.3	36	-	-
20	F	46	**3.33**	**172**	304.8	24	-	

Hemoglobin, hematocrit and MCV in OLP patients.

No.	Sex	Hb g/dl (M=13-18, F=11-16)	Hct. % (M=35-49, F=32-42)	MCV fl (M=82.2-99.5,F=80-97)
1	F	-	40	-
2	F	-	39	-
3	F	15.6	40	98.5
4	F	15.6	48	89
5	M	13.5	41	96.5
6	F	11.8	36	-
7	M	14.9	44	91.8
8	F	12.5	39	96.8
9	F	13.5	40	92.6
10	F	12.3	39	87.4
11	F	14.4	44	78.6
12	F	12.9	37	88.9
13	F	11.1	37	86.9
14	F	11	34	72.9
15	M	14.2	43	96
16	F	13.5	40	93.7
17	F	13.6	38	86.8
18	F	12.1	34	90.5
19	F	10.0	31	62.6
20	F	13.8	44	79.4
21	F	16.1	47	82.4
22	F	14.0	40	79.5

Hemoglobin, hematocrit and MCV in RAU patients

No.	Sex	Hb g/dl (M=13-18, F=11-16)	Hct. % (M=35-49, F=32-42)	MCV fl (M=82.2-99.5,F=80-97)
1	M	-	40	-
2	M	-	47	-
3	M	-	-	-
4	F	14.5	44	83.5
5	F	15.3	44	89.1
6	F	11.9	37	82.9
7	F	13.5	40	88.6
8	F	12.7	36	92.3
9	F	12.4	39	94.9
10	F	12.3	38	99.2
11	F	11.5	35	89.2
12	F	12.5	37	96.3
13	F	12.5	40	97.1
14	M	14.3	40	85.2
15	F	11.8	38	92.3
16	F	12.5	36	82.6
17	F	11.6	36	82.9
18	F	12.9	37	84.6
19	M	14.4	44	92.5

Hemoglobin, hematocrit and MCV in ST/GT patients.

No.	Sex	Hb g/dl (M=13-18, F=11-16)	Hct. % (M=35-49, F=32-42)	MCV fl (M=82.2-99.5,F=80-97)
1	F	-	38	-
2	M	-	43	-
3	F	-	36	-
4	M	-	45	-
5	F	-	43	-
6	F	12.9	40.9	94
7	F	-	38	-
8	F	-	43	-
9	M	14	43	-
10	F	14.9	46.1	-
11	F	-	43	-
12	M	14.4	44	92.5
13	M	**12.5**	36	88.1
14	F	13.2	44	94.4
15	F	12.2	37	90.4
16	F	13.2	38.7	88.8
17	F	**8.2**	**28**	**64.6**
18	F	13.5	37	**79.8**
19	F	12.0	39	81.8
20	F	14.3	42	80.9